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Shortening Self-report Mental Health Symptom Measures through Optimal Test Assembly

Methods: Development and Validation of the Patient Health Questionnaire-Depression-4

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ABSTRACT

Background: The objective of this study was to develop and validate a short form of the Patient Health Questionnaire-9 (PHQ-9), a self-report questionnaire for assessing depressive symptomatology, using objective criteria.

Methods: Responses on the PHQ-9 were obtained from 7,850 English-speaking participants enrolled in 20 primary diagnostic test accuracy studies. PHQ unidimensionality was verified using confirmatory factor analysis, and an item response theory model was fit. Optimal test assembly (OTA) methods identified a maximally precise short form for each possible length between 1 and 8 items, including and excluding the 9th item. The final short form was selected based on pre-specified validity, reliability, and diagnostic accuracy criteria.

Results: A 4-item short form of the PHQ (PHQ-Dep-4) was selected. The PHQ-Dep-4 had a Cronbach's alpha of 0.805. Sensitivity and specificity of the PHQ-Dep-4 were 0.788 and 0.837, respectively, and were statistically equivalent to the PHQ-9 (sensitivity = 0.761, specificity = 0.866). The correlation of total scores with the full PHQ-9 was high ($r = 0.919$).

Conclusion: The PHQ-Dep-4 is a valid short form with minimal loss of information of scores when compared to the full-length PHQ-9. Although OTA methods have been used to shorten patient-reported outcome measures based on objective, pre-specified criteria, further studies are required to validate this general procedure for broader use in health research. Furthermore, due to unexamined heterogeneity, there is a need to

replicate the results of this study in different patient populations.

Introduction

In mental health research and clinical practice, self-report symptom measures are used to assess patient symptoms and identify patients with undetected mental disorders. Completing these measures is demanding, especially when people are asked to respond to multiple measures that each contain multiple items (Coste et al., 1997; Goetz, Lemetayer, & Rat, 2013; Kruiyen, Emons, & Sijtsma, 2013; Stanton, Sinar, Balzer., & Smith, 2002). Therefore, researchers attempt to create shortened versions with scores that perform comparably well with original full-length versions (Coste et al., 1997; Goetz et al., 2013; Kruiyen et al., 2013; Stanton, Sinar, Balzer, & Smith, 2002). (Goetz et al., 2013)

The Patient Health Questionnaire-9 (PHQ-9) is a 9-item, self-report questionnaire that measures depressive symptomatology (Kroenke et al., 2009; Kroenke & Spitzer, 2002; Kroenke, Spitzer, & Williams, 2001). A recent meta-analysis of the PHQ-9 found that at the standard cutoff of 10, based on 34 studies, the sensitivity and specificity were 0.78 and 0.87, respectively (Moriarty, Gilbody, McMillan, & Manea, 2015).

The PHQ-8 is similar to the PHQ-9 and is increasingly used because it eliminates one item that asks about patients' thoughts of either self-harm or being "better off dead" (Kroenke & Spitzer, 2002), but it identifies large numbers of patients not at risk of suicide (Dube, Kroenke, Bair, Theobald, & Williams, 2010; Razykov, Hudson, Baron, & Thombs, 2013). Many studies have reported that the PHQ-8 performs nearly identically to the PHQ-9 (Corson, Gerrity, & Dobscha, 2004; Kroenke & Spitzer, 2002; Leadbeater, Carruthers, Green, Rosser, & Field, 2011; Razykov et al., 2013).

The PHQ-2 is another short-form, designed to include the two core items in a Diagnostic and Statistical Manual of Mental Disorders (DSM) Major Depressive Disorder (MDD) diagnosis: depressed mood and anhedonia (Kroenke, Spitzer, & Williams, 2003). A recent meta-analysis of the PHQ-2 found that at a cutoff of 2, based on 17 studies, the sensitivity and specificity were 0.91 and 0.70, respectively, while at a cutoff of 3, based on 19 studies, the sensitivity and specificity were 0.76 and 0.87, respectively (Manea et al., 2016).

Conventionally, short forms of patient-report measures are created through an expert-based analysis of item content, as with the PHQ-2, or by removing items with minimal factor loadings (Goetz et al., 2013). These methods are not typically applied in a systematic way, and multiple shortened versions of the same measure may exist (Coste et al., 1997; Goetz et al., 2013; Kruyen et al., 2013; Smith, McCarthy, & Anderson, 2000; Stanton, Sinar, Balzer, & Smith, 2002). Methods such as item response theory (IRT; van der Linden & Hambleton, 1997) have been used to evaluate and identify problematic items, but have not incorporated objective and reproducible criteria for item selection.

Optimal test assembly (OTA) is a mixed-integer programming procedures that uses an estimated IRT model to select the subset of items that best satisfies pre-specified constraints (van der Linden, 2006). Although more commonly used in the development of high-stakes educational tests (Holling, Kuhn, & Kiefer, 2013), a recent study demonstrated that OTA can be used to develop shortened versions of patient-reported outcome measures (A. W. Levis et al., 2016). This procedure was also shown to be replicable, reproducible, and produce shortened forms of minimal length as compared with leading alternative methods (Harel & Baron, 2018).

The objective of the present study was to apply OTA to develop a shortened version of the PHQ-9. We (1) used confirmatory factor analysis to verify the unidimensionality of the underlying construct; (2) applied OTA methods to obtain candidate forms of each possible length; and (3) selected the shortest possible form that showed similar performance to the full form in terms of pre-specified validity, reliability, and diagnostic accuracy criteria, compared to the PHQ-9 as the full-form standard.

MATERIALS AND METHODS

This study used a subset of data accrued for an individual participant data meta-analysis (IPDMA) on the diagnostic accuracy of the PHQ-9 depression screening tool to detect major depression (in progress). The IPDMA was registered in PROSPERO (CRD42014010673), and a protocol was published (Thombs et al., 2014).

Search Strategy

A medical librarian searched Medline, Medline In-Process & Other Non-Indexed Citations via Ovid, PsycINFO, and Web of Science (January 2000 - December 2014) on February 7, 2015, using a peer-reviewed search strategy (Supplementary Methods 1). We also reviewed reference lists of relevant reviews and queried contributing authors about non-published studies. Search results were uploaded into RefWorks (RefWorks-COS, Bethesda, MD, USA). After de-duplication, unique citations were uploaded into DistillerSR (Evidence Partners, Ottawa, Canada), for storing and tracking search results.

Identification of Eligible Studies for Full IPDMA

Datasets from articles in any language were eligible for inclusion if they included

diagnostic classifications for current MDD or Major Depressive Episode (MDE) based on a validated semi-structured or fully structured interview conducted within two weeks of PHQ-9 administration, among participants ≥ 18 years and not recruited from youth or psychiatric settings. Datasets where not all participants were eligible were included if primary data allowed selection of eligible participants. For defining major depression, we considered MDD or MDE based on the DSM or MDE based on the International Classification of Diseases (ICD). If more than one was reported, we prioritized DSM over ICD and DSM MDE over DSM MDD. Across all studies, there were 23 discordant diagnoses depending on classification prioritization (0.1% of participants).

Two investigators independently reviewed titles and abstracts for eligibility. If either deemed a study potentially eligible, full-text review was completed by two investigators, independently, with disagreements resolved by consensus, consulting a third investigator when necessary. Translators were consulted to evaluate titles, abstracts and full-text articles.

Data Contribution and Synthesis

Authors of eligible datasets were invited to contribute de-identified primary data. We compared published participant characteristics and diagnostic accuracy results with results from raw datasets and resolved any discrepancies in consultation with the original investigators.

Data Selection for Present Study

We restricted our dataset to participants who completed the PHQ-9 in English, due to the potential for heterogeneity across studies conducted in different languages. We excluded studies that classified major depression using the Mini International Neuropsychiatric Interview (MINI),

because it is structurally different from other fully structured interviews and classifies approximately twice as many participants as cases compared to the most commonly used fully-structured interview, the Composite International Diagnostic Interview (CIDI) (B. Levis et al., Br. J. Psychiatry 2018).

Measure

Scores on each PHQ-9 item reflect frequency of symptoms in the last two weeks and range from 0 (“not at all”) to 3 (“nearly every day”). Higher scores indicate greater depressive symptomatology. Total scores range from 0 to 27 (Kroenke et al., 2001).

Statistical Analyses

Verification of Unidimensionality of the PHQ-9

Robust weighted least squares estimation in Mplus was used to fit a single-factor confirmatory factor analysis model of PHQ-9 items (Muthén & Muthén, 2012). The model was first fit without allowing for any residual correlations among the items. Then modification indices were used to identify item pairs that would improve model fit if their residuals were allowed to correlate, if there was theoretical justification (McDonald & Ho, 2002). Model fit was evaluated concurrently, using: the χ^2 statistic, Comparative Fit Index (CFI), Tucker-Lewis Index (TLI), and Root Mean Square Error of Approximation (RMSEA) (Feinian Chen, Curran, Bollen, Kirby, & Paxton, 2008). Priority was given to CFI, TLI, and RMSEA, because the χ^2 test may reject well-fitting models when sample size is large (Reise, Widaman, & Pugh, 1993). Model fit was considered adequate if CFI and TLI ≥ 0.95 and RMSEA ≤ 0.08 (Hu & Bentler, 1999).

Item Response Theory Model and Optimal Test Assembly

A generalized partial credit model (GPCM) was fit to PHQ-9 (Muraki, 1992). The GPCM is an IRT model that relates a latent trait, representing severity of depressive symptomatology, to the distribution of observed item-level responses. The GPCM estimates two types of item-specific parameters: a discrimination parameter and threshold parameters. From these item-level parameter estimates, item information functions for each item were calculated from the GPCM, as well as a test information function (TIF), obtained by summing item information functions. Because the TIF is inversely related to the standard error of measurement of the latent trait, high amounts of information represent greater precision for measuring depressive symptomatology.

Next, we used OTA, a mixed-integer programming technique to systematically search for the short form that maximized the TIF, subject to the constraint of fixing the number of items included in each short form, optimizing the precision of the short form in estimating participants' level of depressive symptomatology (Boekkooi-Timminga, 1989; van der Linden, 2006). The shape of the TIF was anchored at five points (van der Linden, 2006). Thus, for each short form of lengths 1 to 8 items, OTA selected items from the full set of the nine PHQ-9 items that maximized test information. Due to concerns about the use of the ninth item of the PHQ (Corson et al., 2004; Dube et al., 2010; Lee, Schulberg, Raue, & Kroenke, 2007; Razykov et al., 2013; Rief, Nanke, Klaiberg, & Braehler, 2004), the same procedure was used to generate 8 additional short forms that were forced to exclude the ninth item. In total, the OTA procedure yielded 16 candidate short forms.

For each of the 16 candidate short forms and the full-length form, two scoring procedures were used to obtain estimates of each participant's level of depressive symptomatology. First, the

summed scores across all items included in the short form were calculated. Second, factor scores were estimated for each participant. Although summed scores are typically relied upon for clinical use, the factor scores were considered to provide a better estimate of the latent trait due to well-known limitations of the summed score under the GPCM (Harel, 2014; van der Ark, 2005).

Selection of Final Short Form

The selection of the final short form was based on the following five criteria: reliability, concurrent validity of summed scores, concurrent validity of factor scores, and non-inferior sensitivity and specificity, since the elimination of items necessarily reduces information compared to a full-length form.

Reliability of each candidate short form was assessed with Cronbach's alpha (Cronbach, 1951). The final selected form was required a priori to have a Cronbach's alpha coefficient ≥ 0.80 . Concurrent validity of the summed scores and factor scores was measured with the Pearson's correlation coefficient between the full-length form and candidate short form scores, and were required a priori to be ≥ 0.90 .

Diagnostic accuracy of each candidate short form was assessed through a three-step process. First, the sensitivity and specificity of each candidate short form for each of its possible cutoff summed score values was estimated with a bivariate random-effects model. Second, for each candidate short form, an optimal cutoff score was selected using Youden's J statistic (Youden, 1950). For the full-length form, the conventionally used cutoff score of 10 was selected (Gilbody, Richards, Brealey, & Hewitt, 2007; Kroenke et al., 2001; Kroenke & Spitzer, 2002;

Spitzer et al., 2000; Wittkamp, Naeije, Schene, Huyser, & van Weert, 2007). Third, two non-inferiority tests were conducted for each of the 16 candidate forms to compare sensitivity and specificity, separately, to the full-length form. Non-inferiority tests assess whether the sensitivity or specificity of the short form is not lower than that of the full-length form, up to a pre-specified clinically-significant tolerance (Counsell & Cribbie, 2015), such as $\delta = 0.05$. To conduct the non-inferiority test, the sampling distribution of the test statistic was generated through the bootstrap method (Liu, Ma, Wu, & Tai, 2006). Bootstrapping resamples the original dataset, with replacement, to generate new, artificial, datasets (Efron & Tibshirani, 1994). For each non-inferiority test, 2000 bootstrap iterations were conducted, controlling in each for the number of respondents with and without major depression. For each bootstrap iteration, the bivariate random-effects model was fit to each of the 16 candidate short forms and the full-length form, and the sensitivities and specificities were computed based on their cutoff scores. To account for the multiple testing in the 32 total non-inferiority tests, the Benjamini-Hochberg adjusted p-value was used to determine the significance of the test at the 0.05 significance level (Benjamini & Hochberg, 1995).

The factor analysis was conducted using Mplus 7 (Muthén & Muthén, 2012). All other analyses were conducted using R version 3.3.3 (R Core Team, 2017). The GPCM was fit using the **ltm** package (Rizopoulos, 2006). The OTA analysis was conducted using the **lpSolveAPI** package (Diao & van der Linden, 2011). The bivariate random-effects model was fit using the **lme4** package (Bates, Mächler, Bolker, & Walker, 2015).

RESULTS

Search Results and Inclusion of Primary Data

Of 5,248 unique titles and abstracts identified from the database search, 5,039 were excluded after title and abstract review and 113 after full-text review, leaving 96 eligible articles with data from 69 unique participant samples, of which 55 (80%) contributed datasets (Supplementary Figure 1). Authors of included studies contributed data from three unpublished studies, for a total of 58 datasets. Of these, we excluded 32 studies that administered the PHQ-9 in a language other than English and 6 more that used the MINI. In total, 7,850 participants (863 major depression cases) from 20 primary studies were included. These studies were conducted in the USA, New Zealand, Australia, Canada, the UK, and Cameroon. The mean age of the sample was 33.9 years, and 55.3% of participants were women. See Table 1 for descriptive sample statistics, and Supplementary Table 1 for characteristics of each included study.

Unidimensionality of PHQ-9

A single factor model was fit to the PHQ-9 items with no specification of residual correlations ($\chi^2[df = 36] = 1578.7, p < 0.0001, TLI = 0.966, CFI = 0.974, RMSEA = 0.086$). Modification indices indicated improvement of model fit if residuals of items that measure physical symptoms (items 3, 4, and 5) were correlated. The model was refitted with specification of three correlated residuals, and fit improved ($\chi^2[df = 39] = 750.2, p < 0.0001, TLI = 0.982, CFI = 0.988, RMSEA = 0.062$). Factor loadings for items were all moderately high, with a median of 0.763 and a range of 0.665 to 0.877.

Item Response Theory Model and Optimal Test Assembly

Table 2 presents discrimination parameters for each item based on the GPCM. The item

with the greatest discrimination parameter was item 2. Other items with high values were items 1 and 6. Figure 1 shows the information function of each of the 9 items, as well as the total TIF.

Table 3 shows the items that were included in each of the 16 candidate short forms from the OTA analysis. For the candidate forms generated both with the inclusion of item 9 and without, items 3, 4, and 5 were only selected in the longest short forms, and quickly dropped thereafter. Items 1, 2, and 6 were included in all forms of at least 4 items. For the short forms generated from the full set of nine items, item 9 was included in all candidate short forms.

Selection of final short form

Table 4 presents Cronbach's alpha values and concurrent validity correlations for the 16 candidate short forms. Table 5 presents results of the non-inferiority tests for both sensitivity and specificity. There were four short forms that satisfied our pre-specified criteria in terms of reliability, concurrent validity, and diagnostic accuracy. The four such forms were: 6-item and 7-item short forms that included item 9 and 4-item and 5-item short forms that excluded item 9.

The 4-item short form was the shortest form that fulfilled all criteria. The form includes: item 1 ("Little interest or pleasure in doing things"), item 2 ("Feeling down, depressed, or hopeless"), item 6 ("Feeling bad about yourself – or that you are a failure or have let yourself or your family down"), and item 8 ("Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual"). The PHQ-Dep-4 maintained high reliability with a Cronbach's alpha of 0.805 (95% CI, 0.795, 0.814) compared to 0.866 for the full-length form. Correlations of the summed and factor scores between the PHQ-Dep-4 and PHQ-9 were 0.919 (95% CI, 0.916, 0.923) and

0.910 (95% CI, 0.907, 0.914), respectively. The sensitivity and specificity of the PHQ-Dep-4 at its optimal cutoff of 4 were 0.788 (95% CI, 0.725, 0.840) and 0.837 (95% CI, 0.809, 0.861), respectively. Both sensitivity and specificity were non-inferior to the sensitivity (0.761; 95% CI, 0.679, 0.787) and specificity (0.866; 95% CI, 0.836, 0.892) of the full-length form.

DISCUSSION

This study illustrated how OTA methods can be used to effectively shorten self-report symptom measures while maintaining comparable diagnostic accuracy. OTA methods were applied to shorten the 9-item PHQ-9 to a 4-item version (PHQ-Dep-4). In addition to maintaining similar sensitivity and specificity, the short form had minimal loss of information and maintained reliability and validity that were comparable to the full-length form based on pre-specified criteria. Cronbach's alpha of the PHQ-Dep-4 was 0.805, compared to 0.866 for the full form. Correlations of the summed score and factor score of the PHQ-Dep-4 and PHQ-9 were 0.919 and 0.910, respectively. Per pre-specified criteria, the sensitivity and specificity of the PHQ-Dep-4 (0.788 and 0.837, respectively) were within 5% of those of the PHQ-9 (0.761 and 0.866, respectively).

The 4 items included in the PHQ-Dep-4 included items 1, 2, 6 and 8 from the original PHQ-9. These items included the 2 core depression items (depressed mood and loss of interest) that make up the commonly used PHQ-2. According to diagnostic criteria for major depression, at least one of these symptoms must be present for a diagnosis. The other 2 items in the PHQ-Dep-4 included an affective/cognitive item (feelings of failure) and a somatic item (physical movement). Thus, the PHQ-Dep-4 includes items that qualitatively represent the depressive

symptomatology construct well. We note that the PHQ-Dep-4 includes 1 somatic symptom, whereas the full PHQ-9 includes 4 symptoms. One study found that somatic symptoms may increase scores on the PHQ-9 among somatically ill patients due to factors related to somatic disease, but not depression, among scleroderma patients, but the association was minimal (Leavens, Patten, Hudson, Baron, & Thombs, 2012). Another study, of multiple sclerosis patients, did not find that somatic symptoms influenced scores substantively (Sjonnese et al., 2012).

Both the actual PHQ-2 and the PHQ-8 were selected in the set of 16 candidate short forms. Neither of these, however, were selected by the OTA procedure as optimal. The PHQ-Dep-4 has lower sensitivity than the PHQ-2 (0.788 rather than 0.880), but higher specificity (0.837 rather than 0.725). The PHQ-Dep-4, therefore, may represent a middle ground between shortening the full-length scale, while still retaining desirable measurement and diagnostic properties. The PHQ-Dep-4 may be a useful option in some contexts because it is shorter than the PHQ-9 and PHQ-8, but generates a wider score distribution than the PHQ-2.

There are several limitations for this study that must be considered. First, for the collection of data for the full IPDMA, it was not possible to obtain primary data from 14 of the 69 eligible datasets. Second, the full IPDMA excluded studies where the PHQ-9 was administered exclusively to patients with known psychiatric conditions. Therefore, the generalizability of the results should be confirmed when monitoring treatment response. Third, the present study only included participants for whom the PHQ-9 was administered in English. Fourth, a previous study showed that semi-structured and fully structured interviews have

different characteristics as reference standards (B. Levis et al., *Br. J. Psychiatry* 2018). We excluded studies that used the MINI, given its high rate of diagnosis relative to other diagnostic interviews (B. Levis et al., *Br. J. Psychiatry* 2018). We included studies that used both semi-structured and fully structured interviews as reference standards, and future work should verify that our results apply in both cases. While our dataset included a specific sample of patients, we note that measurement invariance or differential item functioning requirements have been examined in previous studies of the PHQ-9 used as a continuous measure across variables like language (Arthurs, Steele, Hudson, Baron, & Thombs, 2012; Merz, Malcarne, Roesch, Riley, & Sadler, 2013), culture (Baas et al., 2011; Hirsch, Donner-Banzhoff, & Bachmann, 2013; Huang, Chung, Kroenke, Delucchi, & Spitzer, 2006), and medical diagnosis (Chung et al., 2015; Cook et al., 2011; Leavens et al., 2012). These studies provide some degree of confidence that the structure of the PHQ-9 is similar across groups. Lastly, there is a need to replicate our results in different patient populations due to unexamined heterogeneity across the studies included in this analysis.

With regards to the OTA procedure, two limitations must be considered. First, the selection of a short version was sensitive to the choice of criteria for the selection of the final form, and should be carefully considered in future analyses. Additionally, the OTA approach is exploratory and data-driven, and the results of this study should be replicated.

CONCLUSION

The study illustrates how patient self-report symptom measures can be developed and validated using the OTA method, which uses pre-specified objective criteria to determine the

length and specific items that should be included in a short form. The method was implemented with a sample of 7,850 participants from 20 primary PHQ-9 diagnostic studies. The 4-item version was developed and validated based on pre-specified constraints on its test information, reliability, validity, and diagnostic accuracy.

REFERENCES

- Arthurs, E., Steele, R. J., Hudson, M., Baron, M., & Thombs, B. D. (2012). Are Scores on English and French Versions of the PHQ-9 Comparable? An Assessment of Differential Item Functioning. *PLoS ONE*, 7(12), 5–11. <https://doi.org/10.1371/journal.pone.0052028>
- Baas, K. D., Cramer, A. O. J., Koeter, M. W. J., Van De Lisdonk, E. H., Van Weert, H. C., & Schene, A. H. (2011). Measurement invariance with respect to ethnicity of the Patient Health Questionnaire-9 (PHQ-9). *Journal of Affective Disorders*, 129(1–3), 229–235. <https://doi.org/10.1016/j.jad.2010.08.026>
- Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting linear mixed-effects models using lme4. *Journal of Statistical Software*, 67(1). <https://doi.org/10.18637/jss.v067.i01>
- Benjamini, Y., Hochberg, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society*, 57(1), 289–300.
- Boekkooi-timminga, E. (1989). A maximin model for test design. *Psychometrika*, 54(2), 237–247.
- Chung, H., Kim, J., Askew, R. L., Jones, S. M. W., Cook, K. F., & Amtmann, D. (2015). Assessing measurement invariance of three depression scales between neurologic samples and community samples. *Quality of Life Research*, 24(8), 1829–1834. <https://doi.org/10.1007/s11136-015-0927-5>
- Cook, K. F., Bombardier, C. H., Bamer, A. M., Choi, S. W., Kroenke, K., & Fann, J. R. (2011). Do somatic and cognitive symptoms of traumatic brain injury confound depression screening? *Archives of Physical Medicine and Rehabilitation*, 92(5), 818–823. <https://doi.org/10.1016/j.apmr.2010.12.008>
- Corson, K., Gerrity, M. S., & Dobscha, S. K. (2004). Screening for depression and suicidality in a VA primary care setting: 2 items are better than 1 item. *The American Journal of Managed Care*, 10(11 Pt 2), 839–845.
- Coste, J., Guillemin, F., Pouchot, J., & Fermanian, J. (1997). Methodological approaches to shortening composite measurement scales. *Journal of Clinical Epidemiology*, 50(3), 247–252. [https://doi.org/10.1016/S0895-4356\(96\)00363-0](https://doi.org/10.1016/S0895-4356(96)00363-0)
- Counsell, A., & Cribbie, R. A. (2015). Equivalence tests for comparing correlation and regression coefficients. *British Journal of Mathematical and Statistical Psychology*, 68(2), 292–309. <https://doi.org/10.1111/bmsp.12045>

- Cronbach, L. J. (1951). Coefficient alpha and the internal structure of tests. *Psychometrika*, 16(3), 297–334. <https://doi.org/10.1007/BF02310555>
- Diao, Q., & van der Linden, W. J. (2011). Automated test assembly using lp_solve version 5.5 in R. *Applied Psychological Measurement*, 35(5), 398–409. <https://doi.org/10.1177/0146621610392211>
- Dube, P., Kroenke, K., Bair, M. J., Theobald, D., & Williams, L. S. (2010). The P4 screener: Evaluation of a brief measure for assessing potential suicide risk in 2 randomized effectiveness trials of primary care and oncology patients. *The Primary Care Companion to The Journal of Clinical Psychiatry*, 12(June 2008). <https://doi.org/10.4088/PCC.10m00978blu>
- Efron, B., & Tibshirani, R. J. (1994). *An introduction to the bootstrap*. CRC press.
- Feinian Chen, Curran, P. J., Bollen, K. A., Kirby, J., & Paxton, P. (2008). An Empirical Evaluation of the Use of Fixed Cutoff Points in RMSEA Test Statistic in Structural Equation Models. *Sociological Methods & Research*, 36(4), 462–494. <https://doi.org/10.1177/0049124108314720>
- Gilbody, S., Richards, D., Brealey, S., & Hewitt, C. (2007). Screening for depression in medical settings with the Patient Health Questionnaire (PHQ): A diagnostic meta-analysis. *Journal of General Internal Medicine*, 22(11), 1596–1602. <https://doi.org/10.1007/s11606-007-0333-y>
- Goetz, C., Coste, J., Lemetayer, F., Rat, A. C., Montel, S., Recchia, S., ... Guillemin, F. (2013). Item reduction based on rigorous methodological guidelines is necessary to maintain validity when shortening composite measurement scales. *Journal of Clinical Epidemiology*. <https://doi.org/10.1016/j.jclinepi.2012.12.015>
- Harel, D. (2014). The effect of model misspecification for polytomous logistic adjacent-category item response theory models (Doctoral dissertation, McGill University).
- Harel, D., & Baron, M. (2018). Methods for shortening patient-reported outcome measures. *Statistical Methods in Medical Research*. doi: 10.1177/0962280218795187
- Hirsch, O., Donner-Banzhoff, N., & Bachmann, V. (2013). Measurement Equivalence of Four Psychological Questionnaires in Native-Born Germans, Russian-Speaking Immigrants, and Native-Born Russians. *Journal of Transcultural Nursing*, 24(3), 225–235. <https://doi.org/10.1177/1043659613482003>
- Holling, H., Kuhn, J. T., & Kiefer, T. (2013). Optimal test assembly in practice: The design of

- the Austrian educational standards assessment in mathematics. *Journal of Psychology*, 221(3), 190–200.
- Hu, L. T., & Bentler, P. M. (1999). Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling*, 6(1), 1–55. <https://doi.org/10.1080/10705519909540118>
- Huang, F. Y., Chung, H., Kroenke, K., Delucchi, K. L., & Spitzer, R. L. (2006). Using the Patient Health Questionnaire-9 to measure depression among racially and ethnically diverse primary care patients. *Journal of General Internal Medicine*, 21(6), 547–552. <https://doi.org/10.1111/j.1525-1497.2006.00409.x>
- Kroenke, K., & Spitzer, R. L. (2002). The PHQ-9: a new depression diagnostic and severity measure. *Psychiatric Annals*, 32(9), 509–515.
- Kroenke, K., & Spitzer, R. L. (2002). The PHQ-9 : a new depression diagnostic and severity measure. *Psychiatric Annals*, 32(9), 509–515. <https://doi.org/170553651>
- Kroenke, K., Spitzer, R. L., & Williams, J. B. W. (2001). The PHQ-9 Validity of a Brief Depression Severity Measure. *Journal of General Internal Medicine*, 16(9), 605–613. <https://doi.org/10.1046/j.1525-1497.2001.016009606.x>
- Kroenke, K., Spitzer, R. L., & Williams, J. B. W. (2003). The Patient Health Questionnaire-2 Validity of a Two-Item Depression Screener. *Medical Care*, 41(11), 1284–1292. <https://doi.org/10.1097/01.MLR.0000093487.78664.3C>
- Kroenke, K., Strine, T. W., Spitzer, R. L., Williams, J. B. W., Berry, J. T., & Mokdad, A. H. (2009). The PHQ-8 as a measure of current depression in the general population. *Journal of Affective Disorders*, 114(1–3), 163–173. <https://doi.org/10.1016/j.jad.2008.06.026>
- Kruyen, P. M., Emons, W. H. M., & Sijtsma, K. (2013). On the Shortcomings of Shortened Tests: A Literature Review. *International Journal of Testing*. <https://doi.org/10.1080/15305058.2012.703734>
- Leadbeater, E., Carruthers, J. M., Green, J. P., Rosser, N. S., & Field, J. (2011). Nest inheritance is the missing source of direct fitness in a primitively eusocial insect. *Science*, 333(6044), 874–876. <https://doi.org/10.1126/science.1205140>
- Leavens, A., Patten, S. B., Hudson, M., Baron, M., & Thombs, B. D. (2012). Influence of somatic symptoms on patient health questionnaire-9 depression scores among patients with systemic sclerosis compared to a healthy general population sample. *Arthritis Care and Research*, 64(8), 1195–1201. <https://doi.org/10.1002/acr.21675>

- Lee, P. W., Schulberg, H. C., Raue, P. J., & Kroenke, K. (2007). Concordance between the PHQ-9 and the HSCL-20 in depressed primary care patients. *Journal of Affective Disorders*, 99(1–3), 139–145. <https://doi.org/10.1016/j.jad.2006.09.002>
- Levis, A. W., Harel, D., Kwakkenbos, L., Carrier, M. E., Mouthon, L., Poiraudau, S., ... Mills, S. D. (2016). Using Optimal Test Assembly Methods for Shortening Patient-Reported Outcome Measures: Development and Validation of the Cochin Hand Function Scale-6: A Scleroderma Patient-Centered Intervention Network Cohort Study. *Arthritis Care and Research*, 68(11), 1704–1713. <https://doi.org/10.1002/acr.22893>
- Levis, B., Benedetti, A., Riehm, K. E., Saadat, N., Levis, A. W., & Azar, M. (2018). Probability of major depression diagnostic classification using semi-structured versus fully structured diagnostic interviews. *British Journal of Psychiatry*. 212(6), 377-385..
- Liu, J. P., Ma, M. C., Wu, C. Y., & Tai, J. Y. (2006). Test of equivalence and non-inferiority for diagnostic accuracy based on the paired areas under ROC curves. *Statistics in Medicine*, 25(7), 1219–1238. <https://doi.org/10.1002/sim.2358>
- Manea, L., Gilbody, S., Hewitt, C., North, A., Plummer, F., Richardson, R., ... McMillan, D. (2016). Identifying depression with the PHQ-2: A diagnostic meta-analysis. *Journal of Affective Disorders*, 203, 382–395. <https://doi.org/10.1016/j.jad.2016.06.003>
- McDonald, R. P., & Ho, M.-H. R. (2002). Principles and practice in reporting structural equation analyses. *Psychological Methods*, 7(1), 64–82. <https://doi.org/10.1037/1082-989X.7.1.64>
- Merz, E. L., Malcarne, V. L., Roesch, S. C., Riley, N., & Sadler, G. R. (2013). A multigroup confirmatory factor analysis of the Patient Health Questionnaire-9 among English-and Spanish-speaking Latinas. *Cultural Diversity and Ethnic Minority Psychology*, 17(3), 309. <https://doi.org/10.1021/nn300902w>.Release
- Moriarty, A. S., Gilbody, S., McMillan, D., & Manea, L. (2015). Screening and case finding for major depressive disorder using the Patient Health Questionnaire (PHQ-9): A meta-analysis. *General Hospital Psychiatry*, 37(6), 567–576. <https://doi.org/10.1016/j.genhosppsych.2015.06.012>
- Muraki, E. (1992). A Generalized Partial Credit Model : Application of an EM Algorithm. *Applied Psychological Measurement*, 16(2), 159–176.
- Muthén, L., & Muthén, B. (2012). Mplus User’s Guide: Statistical Analysis With Latent Variables. *Mplus User’s Guide (Seventh Edition)*, 1–850. <https://doi.org/10.1111/j.1600-0447.2011.01711.x>

- R Core Team. (2017). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing. Vienna, Austria. Retrieved from <https://www.r-project.org/>
- Razzykov, I., Hudson, M., Baron, M., & Thombs, B. D. (2013). Utility of the Patient Health Questionnaire-9 to assess suicide risk in patients with systemic sclerosis. *Arthritis Care & Research*, 65(5), 753–758. <https://doi.org/10.1002/acr.21894>
- Reise, S. P., Widaman, K. F., & Pugh, R. H. (1993). Confirmatory factor analysis and item response theory: two approaches for exploring measurement invariance. *Psychological Bulletin*, 114(3), 552.
- Rief, W., Nanke, A., Klaiberg, A., & Braehler, E. (2004). Base rates for panic and depression according to the Brief Patient Health Questionnaire: A population-based study. *Journal of Affective Disorders*, 82(2), 271–276. <https://doi.org/10.1016/j.jad.2003.11.006>
- Rizopoulos, D. (2006). ltm: An R package for latent variable modeling and item response theory analyses. *Journal of Statistical Software*, 17(5), 1–25.
- Sjonnesen, K., Berzins, S., Fiest, K. M., Bulloch, A. G. M., Metz, L. M., Thombs, B. D., & Patten, S. B. (2012). Evaluation of the 9–Item Patient Health Questionnaire (PHQ–9) as an Assessment Instrument for Symptoms of Depression in Patients with Multiple Sclerosis. *Postgraduate Medicine*, 124(5), 69–77. <https://doi.org/10.3810/pgm.2012.09.2595>
- Smith, G., McCarthy, D. M., & Anderson, K. (2004). On the sins of short-form development (vol 12, pg 102, 2000). *Psychological Assessment*, 16(3), 340.
- Spitzer, R. L., Kroenke, K., & Williams, J. B. W. (2000). Validation and utility of a self-report version of PRIME-MD. *Primary Care Companion to the Journal of Clinical Psychiatry*, 2(1), 31.
- Stanton, J. M., Sinar, E. F., Balzer, W. K., & Smith, P. C. (2002). Issues and strategies for reducing the length of self-report scales. *Personnel Psychology*, 55(1), 167–194.
- Thombs, B. D., Benedetti, A., Kloda, L. A., Levis, B., Nicolau, I., Cuijpers, P., ... Ziegelstein, R. C. (2014). The diagnostic accuracy of the Patient Health Questionnaire-2 (PHQ-2), Patient Health Questionnaire-8 (PHQ-8), and Patient Health Questionnaire-9 (PHQ-9) for detecting major depression: protocol for a systematic review and individual patient data meta-analysis. *Systematic Reviews*, 3(1), 124. <https://doi.org/10.1186/2046-4053-3-124>
- Van der Ark, L. A. (2005). Stochastic ordering of the latent trait by the sum score under various polytomous IRT models. *Psychometrika*, 70(2), 283–304. <https://doi.org/10.1007/s11336-000-0862-3>

- Van der Linden, W. J. (2006). *Linear models for optimal test design*. New York: Springer.
- Wittkamp, K. A., Naeije, L., Schene, A. H., Huyser, J., & van Weert, H. C. (2007). Diagnostic accuracy of the mood module of the Patient Health Questionnaire: a systematic review. *General Hospital Psychiatry, 29*(5), 388–395.
<https://doi.org/10.1016/j.genhosppsych.2007.06.004>
- Youden, W. J. (1950). Index for rating diagnostic tests. *Cancer, 3*(1), 32–35.
[https://doi.org/10.1002/1097-0142\(1950\)3:1<32::AID-CNCR2820030106>3.0.CO;2-3](https://doi.org/10.1002/1097-0142(1950)3:1<32::AID-CNCR2820030106>3.0.CO;2-3)

Table 1. Patient demographic and diagnostic characteristics (N = 7850)

Sociodemographic variables	Summary
Age, years, <i>mean [median] ± SD (range)</i>	52.0 [54] ± 18.1 (18, 102)
Women, <i>n (%)</i>	4335 (55.2)
PHQ-9 score, <i>mean [median] ± SD (range)</i>	5.2 [3] ± 5.4 (0, 27)
Country, <i>n (%)</i>	
USA	2781 (35.4)
New Zealand	2528 (32.2)
Australia	1092 (13.9)
Canada	573 (7.3)
UK	478 (6.1)
Cameroon	398 (5.1)
Care Setting, <i>n (%)</i>	
Primary care	2928 (37.3)
Non-medical setting	1389 (17.7)
Perinatal care	665 (8.5)
Neurology	607 (7.7)
HIV/AIDS care	398 (5.1)
Oncology	273 (3.5)
Medical rehabilitation	211 (2.7)
Rheumatology	201 (2.6)
Cardiology	100 (1.3)
Stroke care	72 (0.9)
Outpatients with coronary artery disease	1006 (12.8)
Diagnostic Interview, <i>n (%)</i>	
CIDI	3949 (50.3)
SCID	2443 (31.1)
DIS	1006 (12.8)
SCAN	352 (4.5)
DISH	100 (1.3)

Classification system, *n* (%)

DSM-IV	6859 (87.4)
ICD-10	822 (10.5)
DSM-V	169 (2.2)

Table 2. PHQ-9 items and discrimination parameters from the generalized partial credit model

Item Number	Description	Discrimination Parameter
1	Little interest or pleasure in doing things	1.95
2	Feeling down, depressed, or hopeless	2.40
3	Trouble falling or staying asleep, or sleeping too much	0.93
4	Feeling tired or having little energy	1.37
5	Poor appetite or overeating	1.08
6	Feeling bad about yourself – or that you are a failure or have let yourself or your family down	1.90
7	Trouble concentrating on things, such as reading newspaper or watching television	1.41
8	Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	1.29
9	Thoughts that you would be better off dead or of hurting yourself in some way	1.77

Table 3. Items included in optimal short forms of each length with item 9 included and item 9 excluded

Item Number (X indicates inclusion)									
Short	1	2	3	4	5	6	7	8	9
Form	Little	Feeling	Sleep	Feeling	Appetite	Feeling	Concentration	Physical	Thoughts of
Length	interest	down	problem	Tired		failure		Movement	Death or Self-Harm
Item 9 Eligible for Inclusion in Short Forms									
1									X
2		X							X
3	X	X							X
4	X	X				X			X
5	X	X				X		X	X
6	X	X				X	X	X	X
7	X	X		X		X	X	X	X
8	X	X		X	X	X	X	X	X
Item 9 Ineligible for Inclusion in Short Forms									
1		X							
2	X	X							
3	X	X				X			
4	X	X				X		X	
5	X	X				X	X	X	

6	X	X		X		X	X	X
7	X	X		X	X	X	X	X
8	X	X	X	X	X	X	X	X

Table 4. Reliability and validity results of the candidate short forms

Form Length	Cronbach's alpha (95% CI)	Correlation of summed scores (95% CI)	Correlation of factor scores (95% CI)
Item 9 Eligible for Inclusion in Short Forms			
1	NA	0.527 (0.511, 0.543)	NA
2	0.533 (0.504, 0.563)	0.804 (0.796, 0.811)	0.800 (0.792, 0.808)
3	0.727 (0.712, 0.741)	0.863 (0.857, 0.868)	0.869 (0.863, 0.874)
4	0.801 (0.790, 0.810)	0.892 (0.887, 0.896)	0.895 (0.890, 0.899)
5	0.809 (0.799, 0.819)	0.920 (0.916, 0.923)	0.912 (0.909, 0.916)
6	0.835 (0.826, 0.843)	0.939 (0.937, 0.942)	0.931 (0.928, 0.934)
7	0.846 (0.839, 0.854)	0.971 (0.970, 0.973)	0.980 (0.979, 0.980)
8	0.858 (0.851, 0.865)	0.986 (0.986, 0.987)	0.989 (0.989, 0.990)
9	0.866 (0.860, 0.873)	1.000 (1.000, 1.000)	1.000 (1.000, 1.000)
Item 9 Ineligible for Inclusion in Short Forms			
1	NA	0.781 (0.772, 0.79)	NA
2	0.779 (0.763, 0.794)	0.849 (0.842, 0.855)	0.860 (0.855, 0.866)
3	0.816 (0.806, 0.826)	0.887 (0.882, 0.892)	0.891 (0.886, 0.895)
4	0.805 (0.795, 0.814)	0.919 (0.916, 0.923)	0.910 (0.907, 0.914)
5	0.832 (0.824, 0.840)	0.940 (0.936, 0.941)	0.930 (0.927, 0.933)
6	0.845 (0.838, 0.852)	0.970 (0.969, 0.971)	0.978 (0.977, 0.979)
7	0.857 (0.850, 0.863)	0.984 (0.984, 0.985)	0.988 (0.987, 0.988)

8	0.866 (0.860, 0.872)	0.997 (0.997, 0.997)	0.998 (0.998, 0.998)
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Bold values represent those of the final selected form.

Table 5. Diagnostic accuracy results of the candidate short forms and their non-inferiority test results

Form Length	Optimal Cutoff	Sensitivity (95% CI)	P-value	Specificity (95% CI)	P-value
Item 9 Eligible for Inclusion in Short Forms					
1	1	0.420 (0.369, 0.437)	0.976	0.943 (0.930, 0.954)	0.000
2	1	0.929 (0.900, 0.950)	0.000	0.650 (0.592, 0.685)	0.976
3	2	0.892 (0.843, 0.927)	0.000	0.717 (0.680, 0.751)	0.976
4	3	0.858 (0.810, 0.895)	0.000	0.776 (0.744, 0.805)	0.976
5	4	0.806 (0.749, 0.853)	0.000	0.826 (0.798, 0.851)	0.066
6	5	0.837 (0.808, 0.863)	0.000	0.837 (0.808, 0.863)	0.000
7	7	0.814 (0.715, 0.884)	0.000	0.849 (0.820, 0.873)	0.000
8	7	0.856 (0.855, 0.857)	0.000	0.802 (0.801, 0.804)	0.976
9	10	0.761 (0.679, 0.787)	NA	0.866 (0.836, 0.892)	NA
Item 9 Ineligible for Inclusion in Short Forms					
1	1	0.916 (0.877, 0.944)	0.000	0.650 (0.599, 0.698)	0.976
2	2	0.880 (0.825, 0.919)	0.000	0.725 (0.688, 0.760)	0.976
3	3	0.844 (0.796, 0.882)	0.000	0.784 (0.752, 0.813)	0.976
4	4	0.788 (0.725, 0.840)	0.000	0.837 (0.809, 0.861)	0.000
5	5	0.792 (0.716, 0.873)	0.000	0.848 (0.820, 0.873)	0.000
6	6	0.855 (0.762, 0.916)	0.000	0.807 (0.773, 0.838)	0.976
7	7	0.844 (0.762, 0.902)	0.000	0.810 (0.776, 0.840)	0.976

8	8	0.871 (0.786, 0.925)	0.000	0.784 (0.746, 0.819)	0.976
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Bold values represent those of the final selected form.

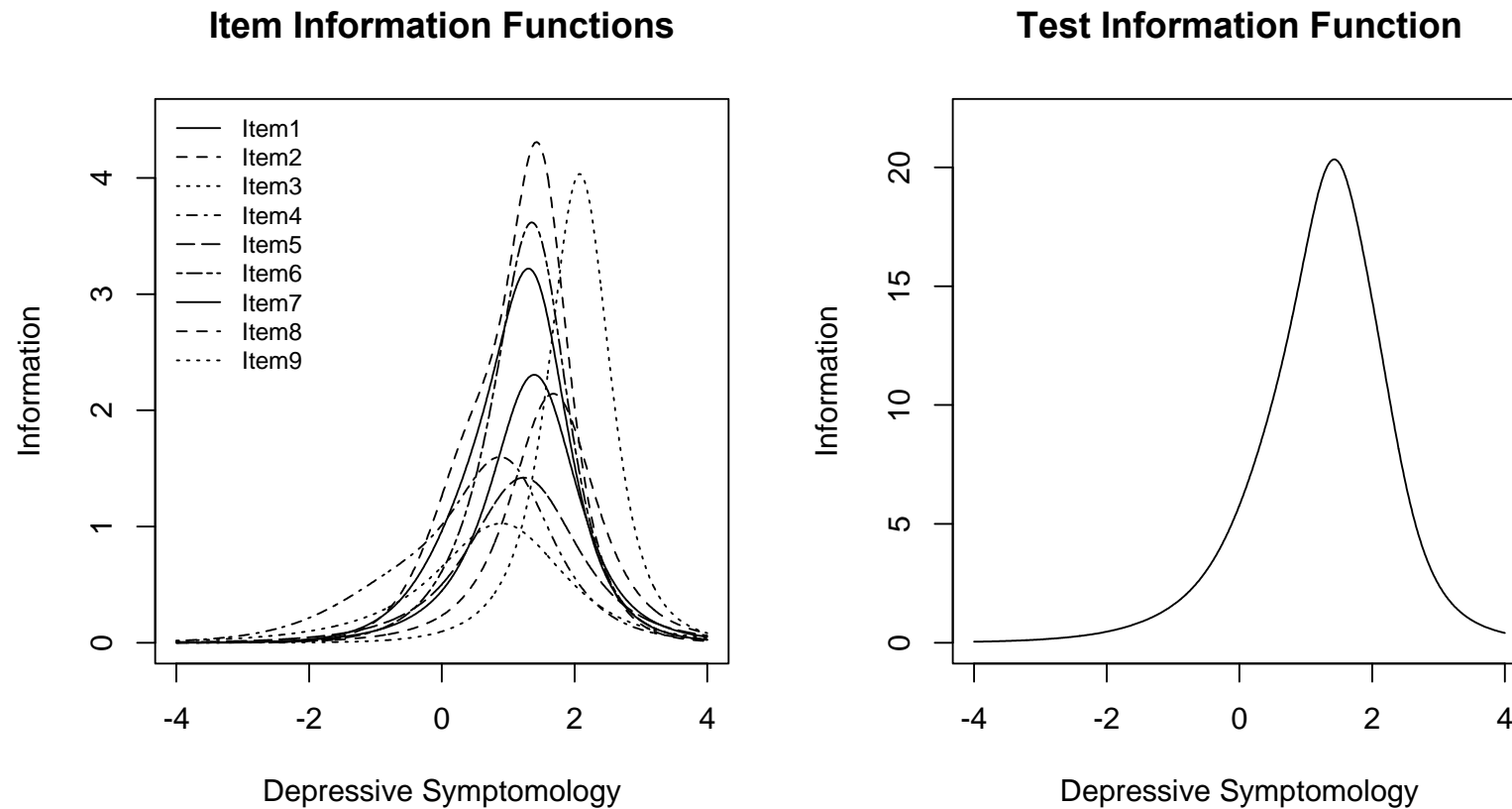
FIGURES

Figure 1. The left hand plot shows the item information functions for each of the 9 items. The right hand plot shows the test information function of the PHQ-9.

Supplementary Material

Supplementary Methods 1. Search Strategies

Supplementary Figure 1. Flow Diagram of Study Selection Process

Supplementary Table 1. Characteristics of included primary studies

Supplementary Table 2. The Patient Health Questionnaire-4 Item Short Form (PHQ-Dep-4)

Supplementary Material References

Supplementary Methods 1. Search Strategies

MEDLINE (OvidSP)

1. PHQ*.af.
2. patient health questionnaire*.af.
3. 1 or 2
4. Mass Screening/
5. Psychiatric Status Rating Scales/
6. "Predictive Value of Tests"/
7. "Reproducibility of Results"/
8. exp "Sensitivity and Specificity"/
9. Psychometrics/
10. Prevalence/
11. Reference Values/
- 12.. Reference Standards/
13. exp Diagnostic Errors/
14. Mental Disorders/di, pc [Diagnosis, Prevention & Control]
15. Mood Disorders/di, pc [Diagnosis, Prevention & Control]
16. Depressive Disorder/di, pc [Diagnosis, Prevention & Control]
17. Depressive Disorder, Major/di, pc [Diagnosis, Prevention & Control]
18. Depression, Postpartum/di, pc [Diagnosis, Prevention & Control]
19. Depression/di, pc [Diagnosis, Prevention & Control]
20. validation studies.pt.
21. comparative study.pt.
22. screen*.af.
23. prevalence.af.
24. predictive value*.af.
25. detect*.ti.
26. sensitiv*.ti.
27. valid*.ti.
28. revalid*.ti.

29. predict*.ti.
30. accura*.ti.
31. psychometric*.ti.
32. identif*.ti.
33. specificit*.ab.
34. cut?off*.ab.
35. cut* score*.ab.
36. cut?point*.ab.
37. threshold score*.ab.
38. reference standard*.ab.
39. reference test*.ab.
40. index test*.ab.
41. gold standard.ab.
42. or/4-41
43. 3 and 42
47. limit 43 to yr="2000-Current"

PsycINFO (OvidSP)

1. PHQ*.af.
2. patient health questionnaire*.af.
3. 1 or 2
4. Diagnosis/
5. Medical Diagnosis/
6. Psychodiagnosis/
7. Misdiagnosis/
8. Screening/
9. Health Screening/
10. Screening Tests/
11. Prediction/
12. Cutting Scores/

13. Psychometrics/
14. Test Validity/
15. screen*.af.
16. predictive value*.af.
17. detect*.ti.
18. sensitiv*.ti.
19. valid*.ti.
20. revalid*.ti.
21. accura*.ti.
22. psychometric*.ti.
23. specificit*.ab.
24. cut?off*.ab.
25. cut* score*.ab.
26. cut?point*.ab.
27. threshold score*.ab.
28. reference standard*.ab.
29. reference test*.ab.
30. index test*.ab.
31. gold standard.ab.
32. or/4-31
33. 3 and 32
38. Limit 33 to “2000 to current”

Web of Science (Web of Knowledge)

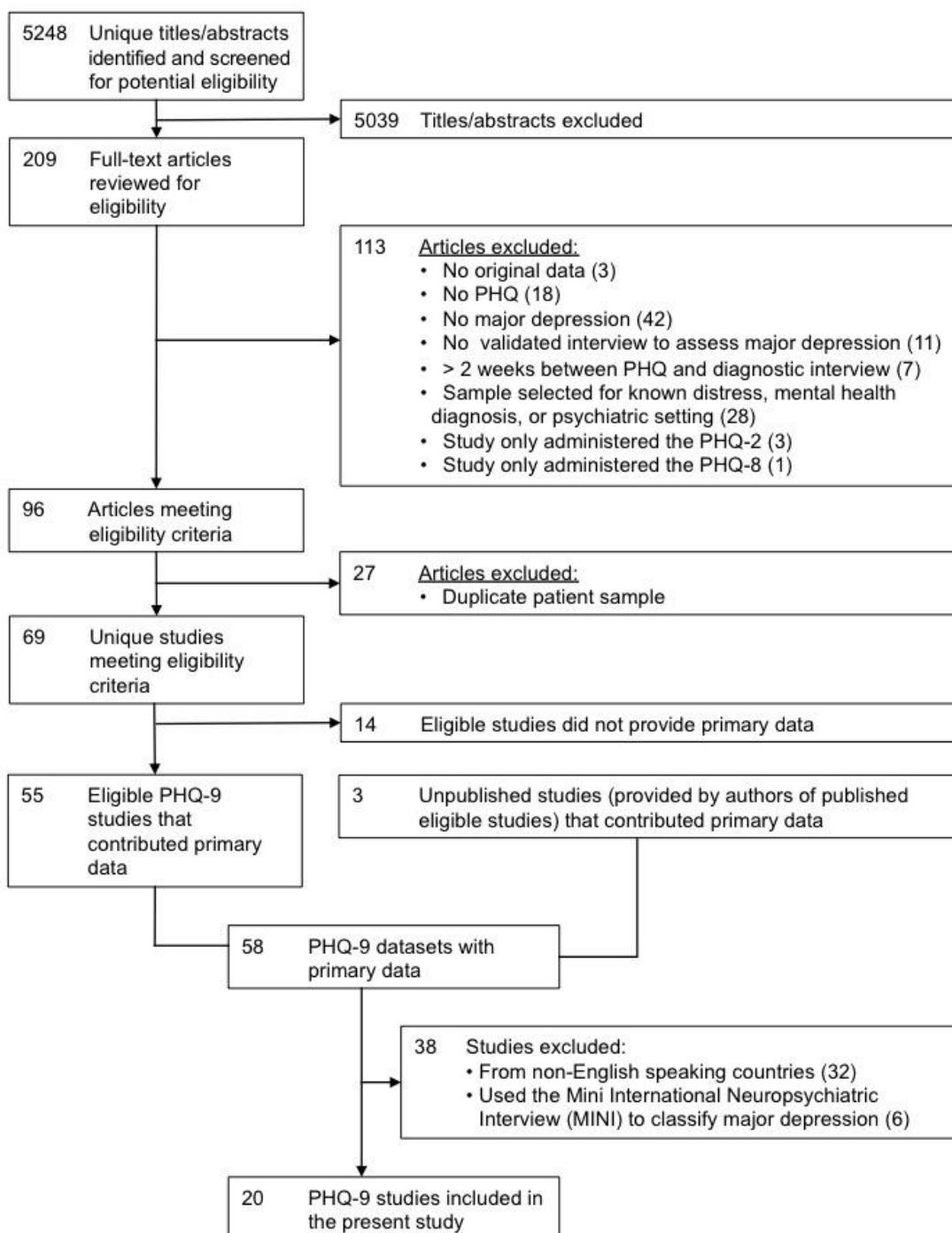
#1: TS=(PHQ* OR “Patient Health Questionnaire”*)

#2: TS= (screen* OR prevalence OR “predictive value*” OR detect* OR sensitiv* OR valid* OR revalid* OR predict* OR accura* OR psychometric* OR identif* OR specificit* OR cutoff* OR “cut off*” OR “cut* score*” OR cutpoint* OR “cut point*” OR “threshold score*” OR “reference standard*” OR “reference test*” OR “index test*” OR “gold standard”)

#1 AND #2

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=2000-2014

Supplementary Figure 1. Flow diagram of study selection process



Supplementary Table 1. Characteristics of included primary studies

First Author, Year	Country	Recruited Population	Diagnostic Interview	Classification System	Total N	Major Depression N (%)
Amoozegar, Unpublished	Canada	Migraine patients	SCID	DSM-IV	203	49 (24)
Arroll, 2010 (1)	New Zealand	Primary care patients	CIDI	DSM-IV	2528	156 (6)
Bombardier, 2012 (2)	USA	Inpatients with spinal cord injuries	SCID	DSM-IV	160	14 (9)
Eack, 2006 (3)	USA	Women seeking psychiatric services for their children at two mental health centers	SCID	DSM-IV	48	12 (25)
Fiest, 2014 (4)	Canada	Epilepsy outpatients	SCID	DSM-IV	169	23 (14)
Gjerdingen, 2009 (5)	USA	Mothers registering their newborns for well-child visits at medical or pediatric clinics	SCID	DSM-IV	419	19 (5)
Kiely, 2014 (6)	Australia	Community sample of adults	CIDI	ICD-10	822	33 (4)
Lambert, 2015 (7)^a	Australia	Cancer patients	SCID	DSM-IV	147	21 (14)
McGuire, 2013 (8)	USA	Acute coronary syndrome inpatients	DISH	DSM-IV	100	9 (9)
Pence, 2012 (9)	Cameroon	HIV-infected patients	CIDI	DSM-IV	398	11 (3)
Razykov, 2013 (10)	Canada	Patients with systemic sclerosis	CIDI	DSM-IV	201	7 (3)
Richardson, 2010 (11)	USA	Older adults undergoing in-home aging services care management assessment	SCID	DSM-IV	377	95 (25)

Rooney, 2013 (12)	UK	Adults with cerebral glioma	SCID	DSM-IV	126	14 (11)
Sidebottom, 2012 (13)	USA	Pregnant women	SCID	DSM-IV	246	12 (5)
Simning, 2012 (14)	USA	Older adults living in public housing	SCID	DSM-IV	190	10 (5)
Thombs, 2008 (15)	USA	Outpatients with coronary artery disease	C-DIS	DSM-IV	1006	221 (22)
Turner, Unpublished	Australia	Cardiac rehabilitation patients	SCID	DSM-IV	51	4 (8)
Turner, 2012 (16)	Australia	Stroke patients	SCID	DSM-IV	72	13 (18)
Twist, 2013 (17)	UK	Type 2 diabetes outpatients	SCAN	DSM-IV	352	79 (22)
Williams, 2012 (18)	USA	Parkinson's disease patients	SCID	DSM-IV	235	61 (26)

Abbreviations: C-DIS: Computerized Diagnostic Interview Schedule; CIDI: Composite International Diagnostic Interview; DISH: Depression Interview and Structured Hamilton; DSM: Diagnostic and Statistical Manual of Mental Disorders; ICD: International Classification of Diseases; PHQ-9: Patient Health Questionnaire-9; SCAN: Schedules for Clinical Assessment in Neuropsychiatry; SCID: Structured Clinical Interview for DSM Disorders; UK: United Kingdom; USA: United States of America.

^aWas unpublished at the time of electronic database search

Supplementary Table 2. The Patient Health Questionnaire-4 Item Short Form (PHQ-DEP-4)

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
4. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual.	0	1	2	3

SUPPLEMENTARY MATERIAL REFERENCES

1. Arroll, B., Goodyear-Smith, F., Crengle, S., Gunn, J., Kerse, N., Fishman, T., ... & Hatcher, S. (2010). Validation of PHQ-2 and PHQ-9 to screen for major depression in the primary care population. *The Annals of Family Medicine*, 8(4), 348-353.
2. Bombardier, C. H., Kalpakjian, C. Z., Graves, D. E., Dyer, J. R., Tate, D. G., & Fann, J. R. (2012). Validity of the Patient Health Questionnaire-9 in assessing major depressive disorder during inpatient spinal cord injury rehabilitation. *Archives of physical medicine and rehabilitation*, 93(10), 1838-1845.
3. Eack, S. M., Greeno, C. G., & Lee, B. J. (2006). Limitations of the Patient Health Questionnaire in identifying anxiety and depression in community mental health: many cases are undetected. *Research on Social Work Practice*, 16(6), 625-631.
4. Fiest, K. M., Patten, S. B., Wiebe, S., Bulloch, A. G., Maxwell, C. J., & Jetté, N. (2014). Validating screening tools for depression in epilepsy. *Epilepsia*, 55(10), 1642-1650.
5. Gjerdingen, D., Crow, S., McGovern, P., Miner, M., & Center, B. (2009). Postpartum depression screening at well-child visits: validity of a 2-question screen and the PHQ-9. *The Annals of Family Medicine*, 7(1), 63-70.
6. Kiely, K. M., & Butterworth, P. (2015). Validation of four measures of mental health against depression and generalized anxiety in a community based sample. *Psychiatry Research*, 225(3), 291-298.
7. Lambert, S. D., Clover, K., Pallant, J. F., Britton, B., King, M. T., Mitchell, A. J., & Carter, G. (2015). Making Sense of Variations in Prevalence Estimates of Depression in Cancer: A Co-Calibration of Commonly Used Depression Scales Using Rasch Analysis. *Journal of the National Comprehensive Cancer Network*, 13(10), 1203-1211.
8. McGuire, A. W., Eastwood, J. A., Macabasco-O'Connell, A., Hays, R. D., & Doering, L. V. (2013). Depression screening: utility of the patient health questionnaire in patients with acute coronary syndrome. *American Journal of Critical Care*, 22(1), 12-19.
9. Pence, B. W., Gaynes, B. N., Atashili, J., O'Donnell, J. K., Tayong, G., Kats, D., ... & Ndumbe, P. M. (2012). Validity of an interviewer-administered patient health questionnaire-9 to screen for depression in HIV-infected patients in Cameroon. *Journal of Affective Disorders*, 143(1), 208-213.

10. Razykov, I., Hudson, M., Baron, M., & Thombs, B. D. (2013). Utility of the Patient Health Questionnaire-9 to Assess Suicide Risk in Patients With Systemic Sclerosis. *Arthritis care & research*, 65(5), 753-758.
11. Richardson, T. M., He, H., Podgorski, C., Tu, X., & Conwell, Y. (2010). Screening depression aging services clients. *The American Journal of Geriatric Psychiatry*, 18(12), 1116-1123.
12. Rooney, A. G., McNamara, S., Mackinnon, M., Fraser, M., Rampling, R., Carson, A., & Grant, R. (2013). Screening for major depressive disorder in adults with cerebral glioma: an initial validation of 3 self-report instruments. *Neuro-oncology*, 15(1), 122-129.
13. Sidebottom, A. C., Harrison, P. A., Godecker, A., & Kim, H. (2012). Validation of the Patient Health Questionnaire (PHQ)-9 for prenatal depression screening. *Archives of Women's Mental Health*, 15(5), 367-374.
14. Simning, A., van Wijngaarden, E., Fisher, S. G., Richardson, T. M., & Conwell, Y. (2012). Mental Healthcare Need and Service Utilization in Older Adults Living in Public Housing. *The American Journal of Geriatric Psychiatry*, 20(5), 441–451.
15. Thombs, B. D., Ziegelstein, R. C., & Whooley, M. A. (2008). Optimizing detection of major depression among patients with coronary artery disease using the patient health questionnaire: data from the heart and soul study. *Journal of General Internal Medicine*, 23(12), 2014-2017.
16. Turner, A., Hambridge, J., White, J., Carter, G., Clover, K., Nelson, L., & Hackett, M. (2012). Depression Screening in Stroke. *Stroke*, 43(4), 1000-1005.
17. Twist, K., Stahl, D., Amiel, S. A., Thomas, S., Winkley, K., & Ismail, K. (2013). Comparison of depressive symptoms in type 2 diabetes using a two-stage survey design. *Psychosomatic Medicine*, 75(8), 791-797.
18. Williams, J. R., Hirsch, E. S., Anderson, K., Bush, A. L., Goldstein, S. R., Grill, S., ... & Pontone, G. (2012). A comparison of nine scales to detect depression in Parkinson disease Which scale to use?. *Neurology*, 78(13), 998-1006.